

## **REMARKS**

Applicants respectfully request reconsideration of the present application in view of the forgoing amendments and in view of the reasons that follow:

### **I. Status of Claims**

1. Claims 1-5, 8, 12, 15-17, 20, 23, 26, 31, 34, 37, 40, 43, 51, 54 and 205-217 are pending in the application.
2. Claim 1 has been amended to put the claim in better condition for appeal and to better define Applicants' invention. Support for the amendment to claim 1 is found in the specification at page 41, lines 14-20; page 43 lines 7-11, Example 1, Table 1 and Example 2.
3. Claims 16 and 17 have been amended to remove redundancies.
4. Applicants' reserve their right to pursue the subject matter of any cancelled claims in one or more continuing applications.

### **II. Request for Continued Examination**

5. A Request for Continued Examination is filed herewith in order to allow the Examiner to consider the references cited on a Supplemental Information Disclosure Statement filed concurrently herewith.

### **III. Oath & Declaration**

6. A new Oath & Declaration will be filed under separate cover.

### **IV. Claim Rejections – 35 USC § 103**

7. Claims 1-5, 8, 12, 15-17, 20, 23, 26, 31, 34, 37, 40, 43, 51, 54 and 205-217 were rejected under 35 USC § 103(a) as being unpatentable over Olson, et al. in view of Pharmacia Fine Chemicals chapter on ion exchange for reasons previously set forth in the Office Action mailed July 12, 2006 and as stated on page 4 of the Office Action mailed on June 12, 2007. Applicants respectfully traverse this rejection.
8. It is respectfully submitted that a *Prima Facie* obviousness rejection has not been made by the combination of the teachings of the Olson, et al. paper and

the Pharmacia Fine Chemicals chapter. The paper of Olson, et al. fails to recognize that the level of aggregate of pegylated protein isoforms will be decreased by separating said isoforms by anion exchange chromatography to less than 6% by weight of the pegylated protein in comparison to the level of aggregate of pegylated protein isoforms present if separated by cation exchange chromatography as described by Olson, et al. further in view of the Pharmacia Fine Chemicals chapter.

Neither does the combination of the teaching of the Pharmacia Fine Chemicals chapter suggest to one of skill in the art the unexpected advantage of using anion exchange chromatography over cation exchange chromatography to reduce the level of aggregate of pegylated protein isoforms as described by the pending claims.

The teachings of Olson, et al. and Pharmacia Fine Chemicals chapter would not have motivated one of skill in the art in seeking to reduce the level of aggregate that a greater decrease in the level of aggregate of pegylated protein isoforms would be achieved by the use of anion exchange resin over the cation exchange resin described by Olson, et al.

In this regard, Applicants direct the Examiner's attention to the advantageous results as provided in Example 1 of Applicants' specification where anion exchange chromatography is utilized in comparison to the results provided in Example 2 of Applicants' specification where cation exchange chromatography is utilized. In particular, the data from Example 2 show resulting aggregate levels higher than the data shown in Example 1.

9. While the paper of Olson, et al., at paragraph bridging pages 171-172, notes that the column chromatography does remove small amounts of high molecular weight cross-linked species. The paper of Olson, et al. does not appreciate that aggregate will remain or be formed at the cation exchange chromatography step as shown by Applicants Example 2.

10. In reference to the comparative data contained in Example 1 and Example 2, Applicants' submit that when a measured property serves to point up a distinction from the prior art or an advantage over the prior art, that property is

relevant to patentability, and its numerical parameter can add precision to the claims for patentability purposes.

11. Further, the claimed invention must be considered as a whole in deciding the question of obviousness. The combination of Olson, et al. and the Pharmacia Fine Chemicals chapter does not teach or suggest to one of ordinary skill in the art the benefit of anion exchange chromatography over cation exchange chromatography to further reduce aggregate levels in the purified product.

12. In response to the Examiner's citation of *In re Aller* it is respectfully submitted that technical details for the process discussed in that opinion are inapplicable to the process of Applicants' invention. While the Examiner notes that the pH for running an anion exchange column differs from the pH used in running a cation exchange column; it was the level of aggregate formation or its reduction which was solved by Applicants' invention. The measurement of aggregate following the cation exchange chromatography was not described in the Olson, et al. paper.

13. Applicants request reconsideration of claims 1-5, 8, 12, 15-17, 20, 23, 26, 31, 34, 40, 43, 51, 54 and 205-217 and the withdrawal of the rejection under 35 U.S.C. § 203.

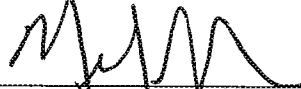
**V. Conclusion**

14. Applicants respectfully submit that all the grounds for rejection of the pending claims have now been overcome and all the claims are in a condition for allowance.

15. An advisory action is requested for the Response After Final Rejection.

16. In the event that the Examiner wishes to discuss any aspect of this response for purposes of advancing the prosecution, please contact the undersigned attorney at the telephone number provided below.

Respectfully submitted,



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